Pergamon

*Tetrahedron Letters*, Vol. 37, No. 32, pp. 5735-5738, 1996

0040-4039/96 $15.00 + 0.00

PII: S0040-4039(96)01213-0

# Cyclopent-2-en-1-ones from [3+2]-Annulation of 3-Ethoxycarbonyl-2-propenylidene(triphenyl)-phosphorane and Glyoxals: Synthesis of *cis*-Jasmone

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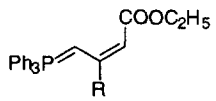
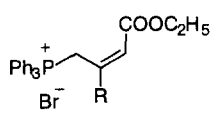
***Abstract***: 3-Ethoxycarbonyl-2-propenylidene(triphenyl)phosphorane (**2**) reacted with glyoxal monohydrates (**5**) to give 2-substituted 5-ethoxycarbonylcyclopent-2-en-1-ones (**6**) by [3+2]-annulation reaction in the presence of a base. Compounds **6** were easily converted to 2-substituted cyclopent-2-en-1-ones by deethoxycarbonylation. An application of the annulation to synthesis of *cis*-jasmone is also described. Copyright © 1996 Elsevier Science Ltd

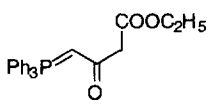
Functionalized five-membered carbocycles are common structural features of many biologically active compounds derived from living systems. Therefore, the formation of substituted cyclopentenones has been an intensely studied subject in recent years,[1] and many approaches of methodological interest have been reported for their preparation.[2] Although five-membered carbocyclic ring formation has been widely studied recently with respect to intramolecular Wittig reactions[3], the synthetic utility of phosphoranes in annulations has been little explored, except for cyclohexadiene formation with α,β-unsaturated aldehydes.



**1**: R=$OC_2H_5$
**2**: R=H



**3**: R=H

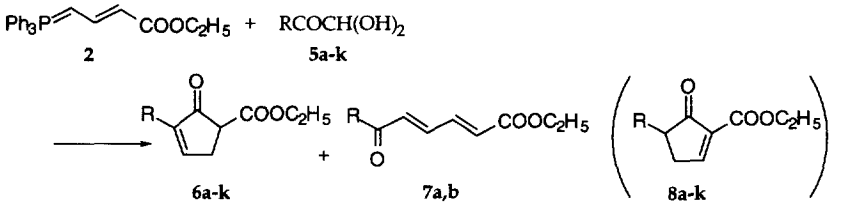


**4**

We have recently reported facile methods for the synthesis of cyclopentadienes from 2-ethoxy-3-ethoxycarbonyl-2-propenylidene(triphenyl)phosphorane (**1**) and α-halo carbonyl compounds[4] and of cyclopent-2-en-1-ones from 3-ethoxycarbonyl-2-oxo-propylidene(triphenyl)phosphorane (**4**) and glyoxal monohydrates (**5**)[5] using [3+2]-annulation. These reactions are shown to proceed regioselectively at the γ-position of the phosphoranes. On the other hand, it has been reported that **1** reacts with **5** to give normal Wittig products, ethyl 6-substituted 3-ethoxy-6-oxo-2,4-hexadienoates (**7**), indicating that the reaction occurs regioselectively at the α-position of the phosphorane **1**.[6] In conjunction with our synthetic studies on [3+2]-annulation of allylidene(triphenyl)phosphoranes and bifunctional carbonyl compounds, we found that reaction of 3-ethoxycarbonyl-2-propenylidene(triphenyl)phosphorane (**2**)[7] with **5** in the presence of a base gave cyclopent-2-en-1-ones **6**, indicating that the reaction occurs regioselectively at the γ-position of the phosphorane **2**. Herein we report an application to synthesis of 2-substituted cyclopent-2-en-1-one by [3+2]-annulation of the phosphorane **2** with **5**.

There are several reports in the literature describing electrophilic capture of phosphorane-stabilized allylic anions by ketones or aldehydes at both the α and γ carbons.[7,8] At first, we examined [3+2]-annulation between the phosphorane **2** and **5a** (Scheme 1).

**Scheme 1**




a: R=4-chlorophenyl,
b: R=H,
c: R=methyl,
d: R=2-pentynyl,
e: R=(S)(-)-$CH_3CH(OTBDMS)CH_2$,
f: R=hexyl
g: R=c-hexyl,
h: R=adamantyl,

j: R=2-naphtyl,
k R=2-furyl,
l: R=2-thienyl

The data shown in Table 1 suggest that the reaction depends on the solvent and the amounts of triethylamine used as a base. Compound **2** reacted with **5a** without the base in THF at room temperature for 1 h to give cyclopent-2-en-1-one **6a** in 4% yield together with the normal Wittig product **7a** in 29% yield, indicating that the reaction occurred predominately at the α carbon.[9]

Table 1. Cyclopent-2-en-1-one **6a** and 2,4-Hexadienoate **7a** from Allylidenephosphorane **2** and Glyoxal Monohydrate **5a**

| Solvent | Mol. ratio of $Et_3N$ | Yield (%)[a,b] | |
|---|---|---|---|
| | | **6a** | **7a** |
| THF | 2.0 | 45 | 18 |
| | 1.0 | 56 | 15 |
| | 0.5 | 33 | 18 |
| | 0.0 | 4 | 29 |
| $CH_2Cl_2$ | 1.0 | 71 | nd[c] |
| | 0.5 | 44 | nd |
| | 0.1 | 33 | nd |
| | 0.0 | 15 | 9 |
| $CH_2Cl_2$-$H_2O$ | excess $NaHCO_3$ | 70 | nd |

[a] Isolated yield. [b] All reactions were carried out by stirring an equimolar mixture of phosphorane **2** and glyoxal monohydrate **5a** in solvent with or without a base at rt for 2 h. Yields are given after chromatography. [c] nd: Not detected.

When the reaction was carried out in the presence of the base in THF, **6a** was obtained in improved yields as the amount of the base was increased. In this case, an equimolar mixture of **2**, **5a**, and triethylamine afforded **6a** in the maximum yield of 56% together with **7a** in 15% yield. When an equimolar mixture of **2** and **5a** was treated with 2 equimolar amount of triethylamine, **6a** was obtained in a reduced yield of 45% together with **7a** in 18% yield. On the other hand, the reaction in dichloromethane ($CH_2Cl_2$) gave **6a** as the main product.

Reaction of an equimolar mixture of **2**, **5a**, and triethylamine gave **6a** in 71% yield without giving the Wittig product **7a**. When an equimolar mixture of **2** and **5a** was treated under two phase conditions of a (1 : 1, v/v) mixture of an aqueous saturated sodium hydrogencarbonate solution and $CH_2Cl_2$, **6a** was obtained in 70% yield without giving **7a**. Under these conditions, **8a**, an isomer of **6a**, was not detected in the reaction mixture.

Compound **6a** was also obtained in good yield by generation of **2** *in situ* by deprotonation of the corresponding phosphonium bromide (**3**) with triethylamine in $CH_2Cl_2$.

Thus, as shown in Table 2, the preparation of **6** by [3+2]-annulation of **2**, prepared *in situ* from **3**, and glyoxal monohydrates **5** except **5b** was achieved in moderate to good yields in the presence of triethylamine in $CH_2Cl_2$. When **2** was allowed to react with **5b** in the presence of the base, the two starting materials disappeared after 1 h-stirring at room temperature, and only unidentified polar oily products were isolated. When an equimolar mixture of **2** and **5b** was stirred without the base, **6b** and **7b** were obtained in very low yields of 4% and 3% yields, respectively. In all runs, **8**, an isomer of **6**, was not detected.

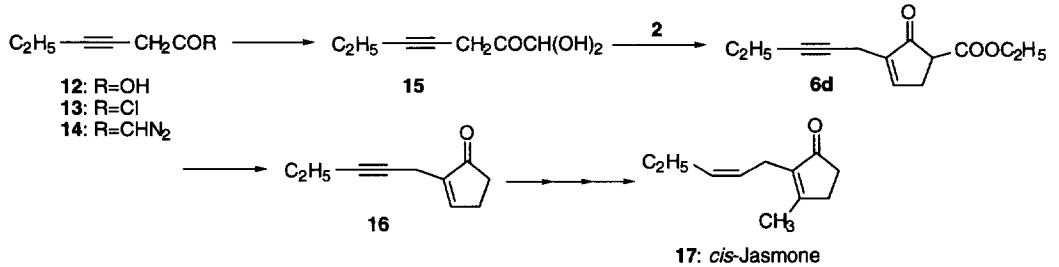
Table 2. 2-Substituted 5-Ethoxycarbonylcyclopent-2-en-1-ones (**6**)

| Compd No. | Yield(%)[a,b] | Compd No. | Yield(%)[a,b] |
|---|---|---|---|
| **6a** | 74 | **6h** | 42 |
| **6c** | 67 | **6i** | 71 |
| **6d** | 55 | **6j** | 85 |
| **6e** | 86 | **6k** | 85 |
| **6f** | 81 | **6l** | 70 |
| **6g** | 41 | | |

[a] Isolated yield. [b] All reactions were carried out by stirring an equimolar mixture of phosphonium bromide **3** and glyoxal monohydrate **5** with two equimolar amount of triethylamine at rt for 2 h in $CH_2Cl_2$. Yields are given after chromatography.

Deethoxycarbonylation[10] of **6** gave cyclopent-2-en-1-ones; that is, **6a** and **6c** reacted with 2 equimolar amount of lithium chloride in the presence of 1 equimolar amount of water in DMSO at 190 ℃ for 2 h gave the corresponding 2-substituted cyclopent-2-en-1-ones[11] in 87% and 73% yields, respectively.

**Scheme 2**




In an application of the annulation, *cis*-jasmone (**17**) was synthesized starting from **6d**, which was prepared by the reaction of **2** with 3-hexynylglyoxal monohydrate (**15**). The reaction sequence is straightforward as illustrated in Scheme 2. Compound **15**, an important key intermediate, was prepared in 80% yield by oxidation of diazoketone **14**, which was prepared *via* 3-hexynoic acid[12] from commercially available 3-hexyn-1-ol, with dimethyl dioxirane in acetone at 0 ℃.[13] Deethoxycarbonylation of **6d** under the conditions described above gave **16**[14] in 71% yield. Conversion of **16** to **17** was accomplished *via* 2',3'-

dehydrojasmone according to the methods in the literature.[14] Thus, **17** was prepared in 29% overall yield from **15**.

In summary, we have demonstrated a new and convenient route to 2-substituted 5-ethoxycarbonyl-cyclopent-2-en-1-ones *via* [3+2]-annulation of 3-ethoxycarbonyl-2-propenylidene(triphenyl)phosphorane and glyoxal monohydrates in the presence of a base. These derivatives were easily converted to 2-substituted cyclopent-2-en-1-ones by deethoxycarbonylation. This method is applicable for the preparation of a variety of 2-substituted cyclopent-2-en-1-ones and related compounds.

## Acknowledgment

The authors are indebted to the Material Analysis Center of ISIR for the elemental analyses.

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9. All new compounds showed the expected spectral properties and gave satisfactory elementary analyses. **6a**: mp 68-69 ℃ (from *iso*-propylether). $^1$H NMR (270 MHz, $CDCl_3$) δ 7.88 (t, 1H, *J*=3.0Hz), 7.64 (d, 2H, *J* = 8.5 Hz), 7.34(d, 2H, *J* =8.5Hz), 4.24(q, 2H, *J* = 7.0 Hz), 3.60 (dd, 1H, *J* = 7.0, 3.0 Hz), 3.10 (dt, 1H, *J* = 20.0, 3.0 Hz), 2.94 (ddd, 1H, *J* = 20.0, 7.0, 3.0 Hz), 1.34 (t, 3H, *J* = 7.0 Hz). $^{13}$C NMR (68 MHz, $CDCl_3$) δ 200.1, 168.7, 158.4, 140.5, 134.6, 129.3, 128.7, 128.3, 61.7, 52.4, 30.4, 14.1. IR (KBr) 1738, 1700, 1620 cm$^{-1}$. MS (EI) m/e 264 ($M^+$). *Anal.* Calcd for $C_{14}H_{13}ClO_3$: C, 63.77; H, 4.59; Cl, 13.44. Found: C, 63.57; H, 4.29; Cl,13.22. Glyoxal monohydrates **5** were prepared by oxidation of diazoketones with 3,3-dimethyldioxirane or DMSO oxidation of acetyl groups.
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(*Received in Japan* 27 *May* 1996; *revised* 13 *June* 1996; *accepted* 17 *June* 1996)